Remarks

This is in response to the Final Office Action mailed March 15, 2006. (Paper No./Mail Date 0206). Applicants note with appreciation the Examiner's careful review of the previously–presented amendments and arguments. Applicants likewise appreciate the professionalism and courtesy of the Primary Examiner at the recent Office Interview.

As set forth in the Office action, the grounds for rejection set forth in the previous Office action, and the status as Final, have been withdrawn.

As the Primary Examiner noted during the Office Interview, previous office actions have rejected the claims based upon Erdelyi alone; Yu alone; Yu, Santagada and Greene; Porcheddu; Porcheddu and Stadler, and Daga and Santagada. Now, in place of the prior grounds of rejection, the claims have been rejected as obvious (none of the claims are rejected as anticipated) under four possible combinations: (i) Yu and Daga; (ii) Yu, Daga, Santagada and Stadler; (iii) Erdelyi and Daga; and (iv) Erdelyi, Daga and Stadler.

Thus, in brief summary, all of the presently-pending obviousness rejections rely upon the Daga reference.

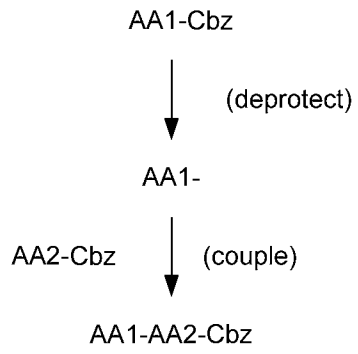
In partial response to the official action, Claim 1 has been amended to recite that successive deprotecting, activating, and coupling steps are carried out in a single vessel without removing the peptide from the single vessel between cycles. This recitation has been in the specification and the claims since filing, but has only been addressed briefly in any of the prior office actions. Keeping the peptide in a single vessel as additional acids are successively added enhances the speed (time) and automation advantages provided by the claimed invention. At the end of each cycle, the partial (or completed) peptide remains in the original vessel ready for the next step without further transfer or handling.

Based upon these and previous amendments, claims 62-82 have been cancelled.

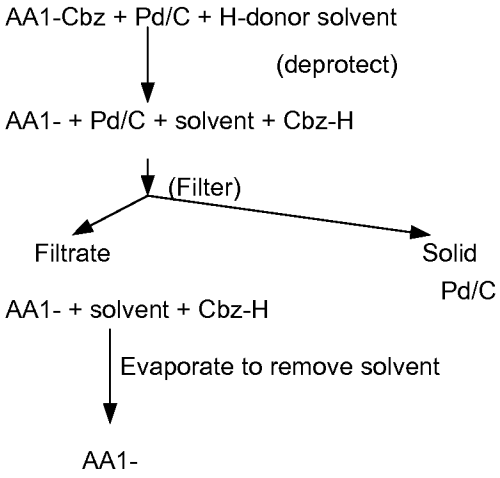
Daga

The Daga reference does not describe peptide synthesis. Daga describes microwave-assisted deprotection of amines protected with benzyl carbamate ("Cbz") groups. If,

however, the skilled person were to extrapolate from Daga to add a hypothetical coupling step, the reaction would proceed as follows:



In order to be fairly evaluated, however, Daga (like any reference) must be viewed in its entirety. When viewed in such context, Daga's deprotecting step always uses a solid catalyst ("Pd/C"). Thus, in more detail the Daga deprotecting step proceeds as follows:



Daga carries out the reaction in an Erlenmeyer flask in a "domestic microwave oven" (page 5191, right hand column). When combined with the application of microwave radiation, the palladium catalyst helps protonate the benzyl carbamate and thus deprotect the

amine. As the diagram indicates, Daga (page 5193) filters the post-microwave product to remove the catalyst and then evaporates the solvent to produce the desired compound.

Based upon Daga's description of the conventional Erlenmeyer flask, the skilled person must assume that the reaction product (filtrate and Pd/C) are transferred to a filter of some sort that retains the Pd/C and passes the filtrate. Thus, the solid palladium catalyst remains with the filter while the liquid filtrate transfers to another vessel or some other fluid flow path. As a result, no further acids can be added to the first acid in the original Erlenmeyer flask (or equivalent vessel). All such additional coupling reactions will require transfer to yet another vessel every time another acid is to be added.

Thus, in order to modify Daga to meet the recitations of Claim 1 (even in combination with other references), the skilled person would have to remove both Pd/C and solvent from Daga's Erlenmeyer flask, while allowing only the decoupled acid to remain. In order to do this in the original flask, the skilled person would need to remove the solid, rather than the filtrate, from the flask.

Daga fails to offer any reason as to why a separation step would be carried out in which the filtrate (rather than the solid) would remain in the original vessel and in which the solid would be removed by some undescribed process.

Stated differently, Daga fails to recognize any disadvantage in removing the deprotected acid from the original deprotection reaction vessel. Having failed to recognize any problem or disadvantage, Daga cannot provide or even suggest a solution to the skilled person.

Because Daga finds no disadvantage in removing the filtrate (deprotected acid and solvent) from the original vessel, Daga cannot suggest any reason to the skilled person as to why the deprotected acid should remain in the original vessel for coupling, and then subsequent deprotection, activation and coupling steps for additional acids.

As another consideration, if Daga uses both a solid phase resin (e.g. compound 13 and the related discussion on page 5193) and a solid phase catalyst, the filtration step Daga describes would fail to separate the deprotected acid from the solid palladium catalyst. Daga

fails to offer any description whatever of whether he made such a separation, and if so how. This lack of information cannot possibly provide the skilled person with the suggestion to carry out the steps now recited in Claim 1.

Absent the Daga reference, the remainder of this combination must logically fail.

Accordingly, because Claim 1 recites the use of the solid phase resin and the use of the single vessel, it recites a combination of steps that are neither disclosed nor suggested by the cited references and the method recited in Claim 1 provides the opportunity for automation by solving problems that the cited references fail to even recognize.

Secondary Considerations

In responding to previous office actions, Applicants have submitted several items of evidence supporting the commercial success (and thus the nonobviousness) of the claimed invention. Applicant respectfully requests that the Examiner consider these again in light of the current amendments and arguments. Additional evidence of commercial success is represented by the article submitted herewith from Genetic Engineering News (July 1, 2006; Volume 26, No. 13) for, "Bioprocessing: Market Growing for Custom-Made Peptides." As set forth on page 3, ("Innovative Technologies"), CEM Corporation, the assignee herein, has placed more than 60 systems according to the claimed invention in academic and industrial research laboratories. Applicants respectfully request that the Examiner give appropriate consideration to this additional evidence of nonobviousness.

Accordingly, Applicants submit that the pending claims define over the rejections as applied in the March 15, 2006 Office Action and Applicants respectfully request that these rejections be removed and the case passed to allowance at the earliest possible date.

Respectfully submitted,

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